

Claims:

1. A recombinant nucleic acid encoding a CAB domain, comprising a portion of calcineurin A and a portion of calcineurin B, wherein the CAB domain forms a tripartite
5 complex with an FKBP/CAB ligand and an FKBP domain.
2. The recombinant nucleic acid of claim 1 wherein the calcineurin A portion of the CAB domain comprises a peptide sequence selected from any of the following peptide sequences: residues 12-394 of human calcineurin A, residues 12-370 of human
10 calcineurin A or residues 340-394 of human calcineurin A.
3. The recombinant nucleic acid of claim 1 wherein the calcineurin B portion of the CAB domain comprises residues 3-170 of human calcineurin B.
- 15 4. The recombinant nucleic acid of claim 1, 2 or 3 comprising a nucleic acid sequence encoding a calcineurin A and/or calcineurin B peptide sequence which differs from a naturally occurring calcineurin peptide sequence by up to ten amino acid substitutions, deletions or insertions.
- 20 5. A recombinant nucleic acid encoding a fusion protein comprising at least one CAB domain of claim 1 and at least one additional domain that is heterologous thereto.
6. The recombinant nucleic acid of claim 5 wherein the heterologous domain is selected from the group comprising a DNA binding domain, a transcription regulatory
25 domain, a cellular localizing domain and a signaling domain.
7. The recombinant nucleic acid of claim 6 wherein the heterologous domain is or is derived from a lexA, GAL4 or composite DNA binding domain.
- 30 8. The recombinant nucleic acid of claim 6 wherein the heterologous domain is or is derived from a p65, VP16 or AP domain.

9. The recombinant nucleic acid of claim 6 wherein the heterologous domain is or is derived from a KRAB domain or a ssr-6/TUP-1 domain.

10. The recombinant nucleic acid of claim 6 wherein the heterologous domain is or is derived from an intracellular domain of a cell surface receptor.

11. A recombinant nucleic acid encoding a fusion protein containing one or more CAB domains which form a tripartite complex with an FKBP domain-containing protein and a non-naturally occurring FKBP/CAB ligand preferentially over FK506.

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12. A nucleic acid composition, comprising a first recombinant nucleic acid of any of claims 5-11 and a second recombinant nucleic acid encoding a fusion protein comprising at least one FKBP domain and at least one additional domain that is heterologous thereto.

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13. A nucleic acid composition of claim 12 wherein the second nucleic acid encodes a fusion protein containing a heterologous domain that is the same or different from the heterologous domain on the first fusion protein.

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14. The nucleic acid composition of claim 13 wherein the first fusion protein comprises a CAB domain and a transcription activation domain and the second fusion protein comprises an FKBP domain and a DNA binding domain.

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15. The nucleic acid composition of claim 13 wherein the first fusion protein comprises a CAB domain and a DNA binding domain and the second fusion protein comprises an FKBP domain and a transcription activation domain.

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16. A nucleic acid composition of claim 12 wherein the first and second fusion proteins form a ligand dependent complex in the presence of ligand, and wherein the complex initiates a detectable biological signal.

17. The nucleic acid composition of claim 16 wherein the biological signal is selected from the group comprising transcription, cell proliferation, cell differentiation, apoptosis.

5 18. The nucleic acid composition of claim 12 wherein the composition further comprises a target gene construct.

19. A fusion protein encoded by the recombinant nucleic acid of any of claims 5-11.

10 20. A vector comprising a recombinant nucleic acid of any of claims 1-3 or 5-11.

21. A vector comprising a recombinant nucleic acid of claim 4.

22. A vector comprising a nucleic acid composition of claim 12.

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23. The vector of claim 20 wherein the vector is a viral vector.

24. The vector of claim 22 wherein the vector is a viral vector.

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25. The vector of claim 23 or 24 wherein the viral vector is selected from the group consisting of adenovirus, AAV, herpesvirus, retrovirus, hybrid adenovirus/AAV, poxvirus, lentivirus.

26. A host cell comprising a recombinant nucleic acid of any of claims 1-3 or 5-11.

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27. A host cell comprising a nucleic acid composition of claim 12.

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28. A host cell cell of claim 26 which is of ~~human~~ origin.

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29. A host cell cell of claim 27 which is of human origin.

30. A host cell of claim 26 which is encapsulated within a biocompatible material.

31. A host cell of claim 27 which is encapsulated within a biocompatible material.

32. A non-human animal containing host cells of claim 26.

33. A non-human animal containing host cells of claim 27.

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34. A method for producing genetically engineered host cells comprising introducing into the cells a recombinant nucleic acid of any of claims 1-3 or 5-11 under conditions permitting DNA uptake by cells.

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10 35. A method for producing genetically engineered host cells comprising introducing into the cells the nucleic acid compositions of any of claims 12-18 under conditions permitting DNA uptake by cells.

36. The method of claim 34 wherein the nucleic acids are introduced ex vivo.

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37. The method of claim 35 wherein the nucleic acids are introduced ex vivo.

38. The method of claim 34 wherein the cells are present within an organism.

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39. The method of claim 35 wherein the cells are present within an organism.

40. A method for multimerizing fusion proteins in the cell of claim 27 which comprises contacting the cells with an effective amount of a ligand under conditions permitting it to form a complex with the fusion proteins.

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41. A method for initiating a detectable biological signal in cells of claim 27 which comprises contacting the cells with a ligand capable of forming a complex with the fusion proteins, in an effective amount permitting gene expression.

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42. A method of claim 40 or 41 wherein the cells are grown in a culture medium and the contacting is effected by adding the ligand to the culture medium.

43. A method of claim 40 or 41 wherein the cells are present within a host organism and the contacting is effected by administering the ligand to the host organism.

44. A method of claim 43 wherein the host organism is a mammal and the ligand is administered by oral, buccal, sublingual, transdermal, subcutaneous, intramuscular, intravenous, intra-joint or inhalation administration in an appropriate vehicle therefor.

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45. A method for providing animal cells responsive to a ligand which comprises introducing into host animal cells a nucleic acid composition of any of claims 12-18.

10 46. A kit which comprises the nucleic acid composition of any of claims 12-18 with an appropriate package insert.

47. A kit of claim 46 which further comprises a ligand capable of forming a complex with the fusion proteins.

15 48. A kit of claim 47 which further comprises a multimerization antagonist.

49. A kit of claim 46 in which one or more of the DNA constructs contains a cloning site in place of a heterologous domain.

20 50. A kit of claim 46 in which the target gene construct contains a cloning site in place of a target gene.

49 51. A kit of claim 46 in which the target gene construct contains a cloning site in place of a target gene.